REMARKS

Claims 25-30 are pending in this Application.

Double Patenting

Applicant respectfully requests that this issue be deferred until an allowable subject matter is indicated.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 25-30 are rejected under 35 U.S.C. §112, first paragraph, allegedly because "the specification does not reasonably provide enablement for treating ischemia reperfusion injury with alpha 1-antitrypsin, alpha 1-antitrypsin-like agents, antielastase or antiproteinase-3agens [sic]; the additional administration of a thrombolytic agent, and the additional use of a mechanical device to reestablish blood flow." See page 3 of the Office Action. In particular, the Office Action alleges that "The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation...." See page 4 of the Office Action.

The first paragraph of §112 requires that the disclosure of a patent application be such that persons skilled in the art, having read the patent application, would be able to practice the inventions described by the claims. There is no legal requirement that this be done in any particular manner; an enabling disclosure can be provided by the use of illustrative examples or simply by broad terminology. *In re Marzocchi*, 169 U.S.P.Q. 367 (C.C.P.A. 1971). Moreover, a patent application must be deemed to be enabling unless there is reason to doubt the truth of statements contained in the patent application relating to making and using the invention. *Id.,* 169 U.S.P.Q. at 369-370.

Furthermore, when rejecting a claim under the enablement requirement of §112, the Patent Office bears the "initial burden of setting forth a reasonable explanation as to why...the scope of protection provided by [the] claim is not adequately enabled by the description of the invention provided in the specification." *In re Wright*, 27 U.S.P.Q.2d. 1510, 1513 (Fed. Cir. 1993). To object to a specification on the grounds that the disclosure is not enabling with respect to the scope of a claim sought to be patented, the Examiner must provide evidence or technical reasoning substantiating those doubts. *Id.*; and *M.P.E.P.* §2164.04. Without a reason to doubt

the truth of the statements made in the patent application, the application must be considered enabling. *In re Wright*, 27 U.S.P.Q. 2d at 1513; *In re Marzocchi*, 169 U.S.P.Q. at 369.

It is noted that the Office Action does not provide any evidence or technical reasoning substantiating this alleged nonenablement. The Office Action simply concludes that "The present invention is unpredictable unless experimentation is shown for the treat [sic] of ischemia reperfusion injury with all the compounds of claim 1, along with all thrombolytic agents, and all mechanical device [sic] for reestablishing blood flow." Page 4 of the Office Action.

It is well established, however, that a patent is not rendered nonenabling merely because there can be no guarantee that particular examples would actually work. *Atlas Powder Company v. EI Dupont d Nemours and Company*, 224 USPQ 409 (C.A.F.C. 1984). Moreover, the mere possibility that a claim embraces inoperable species does not render it unduly broad. In *re Kamal*, et al., 158 U.S.P.Q. 320 (C.C.P.A. 1968); *ex parte Clark et al.*, 174 U.S.P.Q. 40 (P.O.B.A. 1971). It is not a function of the claims to specifically exclude possible inoperative species. *In re Dinh-Nugyen* et al., 181 U.S.P.Q. 46 (C.C.P.A. 1974); *Ex parte Janin*, 209 U.S.P.Q. 761 (P.O.B.A. 1979); *Ex parte Jackson*, 217 U.S.P.Q. 804 (P.O.B.A. 1982). It should also be noted that there is no requirement in the patent law that every representative compound has to be explicitly disclosed or exemplified in the specification.

More significantly, the Examiner fails to provide any evidence to doubt that Applicant's disclosure would enable those skilled in the art to practice the claimed invention. Thus, rejection of claims for alleged lack of enablement is improper.

It appears the Examiner apparently finds fault with the specification because Applicant has not provided working examples for "all compounds of claim 1, along with all thrombolytic agents, and all mechanical [devices] for reestablishing blood flow." Page 4 of the Office Action. This fact, however, does not provide any reason to doubt that those skilled in the art having the present patent application before them would be able to practice the claimed inventions. It is well established that a working example is not mandatory and that all that is required is that the invention be disclosed so that one skilled in the art can practice it without undue experimentation. *In re Borkowski* et al., 164 USPQ 642 (C.C.P.A. 1970); *Ex parte Krenzer*, 199 USPQ 227 (P.O.B.A. 1978). Indeed, the court in *re Fouche* specifically found that an Applicant need not include working examples of the Markush members:

> Appellant is quite correct in contending that, under our decisions in *In re Robins* . . . the inclusion of representative examples is ***not*** required to enable a person skilled in the art to use a generic invention.

In re Fouche, 169 U.S.P.Q. 429, 443 (C.C.P.A. 1971) (citations omitted, emphasis added).

It is well established that the patent office has the burden of showing that the disclosure entails undue experimentation. *In re Angstadt*, 190 USPQ 214 (C.C.P.A. 1976).

In the present case, the Examiner has failed to do so. The Examiner simply concludes that the scope of the claims is broader than the scope of the enablement because "The claims are inclusive to all α1-antitrypsins, α1-antitrypsin-like agents, antielastase, or antiproteinase-3 agents, or combinations thereof; all thrombolytic agents and all mechanical devices for reestablishing blood flow." Page 4 of the Office Action. It is interesting contradiction in the Office Action that the Examiner acknowledges "The relative skill of those in the art is generally that of a Ph.D. or M.D." *Id.*

As admitted by the Examiner, "The relative skill of those in the art is generally that of a Ph.D. or M.D." Accordingly, Applicant submits that in view of the guidance provided by the present patent application, one of ordinary skill in the art would have the necessary medical knowledge to practice the methods of the present invention without undue experimentation. For example, in contrast to the Examiner's unsubstantiated assertion one skilled in the art would readily recognize that not all "α1-antitrypsins, α1-antitrypsin-like agents, antielastase, or antiproteinase-3 agents, or combinations thereof; all thrombolytic agents and all mechanical devices for reestablishing blood flow" would be useful in methods of the invention.

Since the Examiner fails to provide any reasonable evidence to doubt that Applicant's disclosure would enable those skilled in the art to practice the claimed invention, the rejection under alleged lack of enablement is improper and should be withdrawn.

Moreover, it is submitted that the specification provides ample teaching to enable one skilled in the art to treat ischemia reperfusion injury using compositions claimed in Claim 25. For example, page 22, line 18, to page 23, line 13, of the specification discloses treating ischemia reperfusion injury using methods of the invention. See, also, original claim 20. Thus, the specification has clearly enabled one skilled in the art to use the compositions of the present invention in treating ischemia reperfusion injury.

Thus, the rejection of claims under 35 U.S.C. §112, first paragraph, is without any merit. Accordingly, Applicants request withdrawal of the rejections under 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §103

Claims 25 and 28 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Gyorkos et al. (US Patent No. 5,618,792) in view of Szabo et al., *FEBS Letters*, **1995**, *372*, 229-232 (the "Szabo et al. Reference"), and further in view of US Patent Application Publication No. 2004/0132666 to Neuwelt et al. (the "Neuwelt et al. Patent Application").

Claims 25-26 and 28 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the Gyorkos et al. Patent, the Szabo et al. Reference and Neuwelt et al. Patent Application as applied to claims 25 and 28 above in view of Verstraete, *Eur. Heart Journal*, **1985**, *6*, 586-593 (the "Verstraete Reference").

Claims 25-28 and 30 are rejected under 35 U.S.C §103(a) as allegedly being unpatentable over the Gyorkos et al. Patent, the Szabo et al. Reference and the Neuwelt et al. Patent Application as applied to claims 25 and 28, and further in view of U.S. Patent No. 5,180,366, issued to Woods (the "Woods Patent").

One of the crucial basis of the rejections under 35 U.S.C. §103(a) appears to be that the Szabo et al. Reference teaches one skilled in the art to include a free radical scavenger. For example, the Office Action states that:

> **The instant invention differs from the cited references in that the cited reference does not teach the administration of a free radical scavenger such as dihydrorhodamine.** Szabo et al. teach the administration of dihydrorhodamine in vivo to rats which have induced splanchnic ischemica and reperfusion…and further teach that peroxynitrite…is formed during ischemia and reperfusion…as well as that the early formation of peroxynitrite **necessitates the introduction of different therapeutic strategies**….
>
> One of ordinary skill in the art would have been motivated to combine the references [the Gyorkos et al. Patent and the Szabo et al. Reference] because all are directed to the treatment of ischemia and/or reperfusion.

(Emphasis added). Page 8 of the Office Action.

Without commenting on the propriety of other cited references, as discussed in detail below, it is submitted that the Szabo et al. Reference does not teach administering a free radical scavenger such as dihydrorhodamine to treat ischemia reperfusion injury. As the Szabo et al.

Reference clearly states, the reason for administering dihydrorhodamine 123 (i.e., DHR 123, a free radical scavenger) is to measure the amount of peroxynitrite production during shock not to treat ischemia reperfusion injury. See, for example, the Abstract ("To quantify peroxynitrite production during shock, we measured oxidation of dihydrorhodamine 123 in rats...."). See, also, the Introduction section ("The oxidation of dihydrorhodamine 123 to rhodamine has been used in in vitro experiments to measure the production of peroxynitrite.... In the present study, we have made an attempt to utilize the oxidation of dihydrorhodamine 123 to rhodamine to estimate the formation of biologically active peroxynitrite in vivo." (emphasis added)). See, also, page 232 ("Measuerement of NOS-inhibitor-inhibitable **oxidation of dihydrorhodamine may be useful in investigating peroxynitrite formation** in pathophysiological conditions associated with •NO and superoxide production." (emphasis added)).

Furthermore, the Materials and methods section clearly shows, that DHR 123 is not used to treat ischemia reperfusion injury. For example, all the animals were sacrificed after administration of DHR 123. See Materials and methods section. It seems highly unlikely that sacrificing the animals after administration of DHR 123 can be interpreted as a means for determining ischemia reperfusion injury treatment.

As it is clearly evident from above, the Szabo et al. Reference uses DHR 123 as a means for quantifying the amount of peroxynitrite formation and not for any treatment purposes. In view of the above, it is abundantly clear that one of the most crucial arguments relied upon in the Office Action for the 35 U.S.C. §103(a) rejection is erroneous. Hence, it is respectfully submitted that all of the rejections under 35 U.S.C. §103(a) is improper. Accordingly, it is respectfully requested that all of the rejections under 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

In view of the foregoing, it is respectfully submitted that the claims presently before the Examiner patentably define the invention over the applied art and are otherwise in condition for allowance. Therefore, an early Office Action to that effect is earnestly solicited. In the event that a telephone conversation would further prosecution and/or expedite allowance, the Examiner is invited to contact the undersigned.

Respectfully submitted,

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